IUCLID

Data Set

Existing Chemical	:	ID: 3622-84-2
CAS No.	:	3622-84-2
EINECS Name	:	N-butylbenzenesulphonamide
EC No.	:	222-823-6
TSCA Name	:	Benzenesulfonamide, N-butyl-
Molecular Formula	:	C10H15NO2S

Producer related part

Company	:	Proviron Fine Chemicals N.V.
Creation date	:	14.01.2002 (by Notox)

Substance related part

Company	:	Proviron Fine Chemicals N.V.
Creation date	:	14.01.2002 (by Notox)
Status	:	
Memo	:	
Printing date	:	31.05.2005
Revision date	:	
Date of last update	:	31.05.2005
Number of pages	:	377
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	Manufacturer
Name	:	Proviron Fine Chemicals N.V.
Contact person	:	Vincent Acou
Date	:	
Street	:	Stationsstraat 123 bus 2
Town	:	8400 Oostende
Country	:	Belgium
Phone	:	+32 59 56 21 00
Telefax	:	+32 59 56 21 30
Telex	:	
Cedex	:	
Email	:	vincent.acou@proviron.com
Homepage	:	

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1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

Type	:	Manufacturer
Name of plant	:	Proviron Fine Chemicals N.V.
Street	:	Stationsstraat 123 bus 2
Town	:	8400 Oostende
Country	:	Belgium
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

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1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	N-n-Butylbenzenesulphonamide
Smiles Code	:	O=S(=O)(NCCCC)c(cccc1)c1
Molecular formula	:	C10H15NO2S
Molecular weight	:	213.3
Petrol class	:	

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1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	

Substance type	:	Organic
Physical status	:	Liquid
Purity	:	>= 99 % w/w
Colour	:	
Odour	:	

Reliability : The slight haematological deviations which occurred only in males were not considered to be treatment related. Hyaline droplets in the kidney is considered to be specific for male rats and not relevant to humans. The NOAEL = 50 mg/kg bw based on effects on liver and low incidence of degenerating nerve fibres.

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1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

BBSA; n-Butylamide of benzenesulphonic acid

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1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

Quantity : 1000 - 5000 tonnes produced in 1995

Flag : Confidential
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Quantity : 1000 - 5000 tonnes produced in 1996

Flag : Confidential
31.05.2005

Quantity : 1000 - 5000 tonnes produced in 1997

Flag : Confidential
31.05.2005

Quantity : 2000 - 4000 tonnes produced in 1998

Flag : Confidential
31.05.2005

Quantity : 2000 - 4000 tonnes produced in 1999

Flag : Confidential
31.05.2005

Quantity : 2000 - 4000 tonnes produced in 2000

Flag : Confidential
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1.6.1 LABELLING

Labelling : provisionally by manufacturer/importer
Specific limits :

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1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

Type of use : Type
Category : Use resulting in inclusion into or onto matrix

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Type of use : Industrial
Category : other: plastifier

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Type of use : Industrial
Category : other: smelting agents for moulding

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1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

Remark	:	Human exposure : scarce, unless the material is applied hot (vapours may be hazardous). Environment : potentially not affected. Production process : by reaction of benzenesulphonul chloride with n-butylamine. (one site of production at Proviron Fine Chemicals in BE)
Source 10.12.2003	:	Proviron Fine Chemicals N.V. Oostende

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	= -30 °C
Sublimation	:	
Method	:	other: ISO 1392
Year	:	1991
GLP	:	no
Test substance	:	
Test substance	:	BBSA (CAS 3622-84-2)
Reliability	:	(4) not assignable
23.05.2005		(1) (2)

2.2 BOILING POINT

Value	:	> 250 °C at 1013 hPa
Test substance	:	BBSA (CAS 3622-84-2)
Reliability	:	(4) not assignable
23.05.2005		(1)
Value	:	= 190 - 195 °C at 5 hPa
Test substance	:	BBSA (CAS 3622-84-2)
Reliability	:	(4) not assignable
23.05.2005		(3) (2)

2.3 DENSITY

Type	:	relative density
Value	:	ca. 1.147 g/cm³ at 20 °C
Method	:	other: ISO 758
Year	:	1991
GLP	:	no
Test substance	:	
Test substance	:	BBSA (CAS 3622-84-2)
Reliability	:	(4) not assignable
23.05.2005		(4)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	= .000056 hPa at 25 °C
Decomposition	:	
Method	:	other (measured): Modified Grain Method
Year	:	2005
GLP	:	
Test substance	:	
Result	:	4.21E-05 mmHg = 5.6E-05 hPa
Test substance	:	BBSA (CAS 3622-84-2)

Reliability : (2) valid with restrictions
23.05.2005 (5)

Value : < .001 hPa at 20 °C

Remark : Estimated value.
Test substance : BBSA (CAS 3622-84-2)
Reliability : (4) not assignable
23.05.2005 (3)

Value : < .1 hPa at 20 °C

Remark : Estimated value.
Test substance : BBSA (CAS 3622-84-2)
Reliability : (4) not assignable
23.05.2005 (6)

Value : < .2 hPa at 20 °C

Remark : Estimated value.
Test substance : BBSA (CAS 3622-84-2)
Reliability : (4) not assignable
23.05.2005 (1)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : = 2.1 at °C
pH value :
Method : other (calculated)
Year : 2001
GLP : yes
Test substance :

Method : Rekker calculation method
Test substance : BBSA (CAS 3622-84-2)
Reliability : (2) valid with restrictions
23.05.2005 (7)

Partition coefficient : octanol-water
Log pow : = 2.3 at °C
pH value :
Method : other (calculated)
Year :
GLP :
Test substance :

Test substance : BBSA (CAS 3622-84-2)
Reliability : (2) valid with restrictions
23.05.2005 (8)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in : Water
Value : at °C
pH value :
concentration : at °C
Temperature effects :

Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other
Year	:	
GLP	:	
Test substance	:	

Result	:	insoluble
Reliability	:	(4) not assignable

23.05.2005 (1) (6) (3) (2)

Solubility in	:	Water
Value	:	ca. 1.02 at 20 °C
pH value	:	ca. 6.7
concentration	:	1.02 g/l at 20 °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	

Test substance	:	BBSA (CAS 3622-84-2)
Reliability	:	(4) not assignable

23.05.2005 (1)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value	:	>= 200 °C
Type	:	open cup
Method	:	other: ISO 2719
Year	:	1991
GLP	:	no
Test substance	:	

Test substance	:	BBSA (CAS 3622-84-2)

14.05.1998 (4)

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

INDIRECT PHOTOLYSIS

Sensitizer	:	OH
Conc. of sensitizer	:	1500000
Rate constant	:	= .00000000001383 cm³/(molecule*sec)
Degradation	:	50 % after 9.3 hour(s)
Deg. product	:	
Method	:	other (calculated)
Year	:	2005
GLP	:	
Test substance	:	

Result : AOP Program (v1.91) Results:

==========

SMILES : O=S(=O)(NCCCC)c(cccc1)c1
CHEM : Benzenesulfonamide, N-butyl-
MOL FOR: C10 H15 N1 O2 S1
MOL WT : 213.30
SUMMARY (AOP v1.91): HYDROXYL RADICALS
Hydrogen Abstraction = 13.4132 E-12 cm3/molecule-sec
Reaction with N, S and -OH = 0.0000 E-12 cm3/molecule-sec
Addition to Triple Bonds = 0.0000 E-12 cm3/molecule-sec
Addition to Olefinic Bonds = 0.0000 E-12 cm3/molecule-sec
**Addition to Aromatic Rings = 0.4169 E-12 cm3/molecule-sec
Addition to Fused Rings = 0.0000 E-12 cm3/molecule-sec

OVERALL OH Rate Constant = 13.8300 E-12 m3/molecule-sec
HALF-LIFE = 0.773 Days (12-hr day; 1.5E6 OH/cm3)
HALF-LIFE = 9.281 Hrs

SUMMARY (AOP v1.91): OZONE REACTION

****** NO OZONE REACTION ESTIMATION ******
(ONLY Olefins and Acetylenes are Estimated)

Experimental Database: NO Structure Matches

Test substance : BBSA (CAS 3622-84-2)
Reliability : (2) valid with restrictions
23.05.2005 (5)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C
t1/2 pH9	:	at °C
Deg. product	:	
Method	:	other
Year	:	2005
GLP	:	
Test substance	:	

Remark : Hydrolysis cannot be measured due to the low water solubility.
Model calculations are only able to estimate the hydrolysis rate for Esters, Carbamates, Epoxides, Halomethanes (containing 1-3 halogens) and Specific Alkyl Halides.

Test substance : BBSA (CAS 3622-84-2)
31.05.2005 (5)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type : fugacity model level III
Media :
Air : % (Fugacity Model Level I)
Water : % (Fugacity Model Level I)
Soil : % (Fugacity Model Level I)
Biota : % (Fugacity Model Level II/III)
Soil : % (Fugacity Model Level II/III)
Method : other: calculated
Year : 2005

Result : Chem Name : Benzenesulfonamide, N-butyl-
Molecular Wt: 213.3
Henry's LC : 2.17e-006 atm-m3/mole (Henrywin program)
Vapor Press : 4.21e-005 mm Hg (Mpbpwin program)
Liquid VP : 0.000279 mm Hg (super-cooled)
Melting Pt : 108 deg C (Mpbpwin program)
Log Kow : 2.31 (Kowwin program)
Soil Koc : 83.7 (calc by model)

	Mass Amount (percent)	Half-Life (hr)	Emissions (kg/hr)
Air	0.0445	18.6	0
Water	99.4	360	1000
Soil	0.0493	720	0
Sediment	0.519	3.24e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (percent)	Advection (percent)
Air	1.73e-013	5.67	1.52	0.567	0.152
Water	1.73e-011	653	339	65.3	33.9
Soil	4.12e-014	0.162	0	0.0162	0
Sediment	1.5e-011	0.379	0.0354	0.0379	0.00354

Persistence Time: 341 hr
Reaction Time: 518 hr
Advection Time: 1e+003 hr
Percent Reacted: 65.9
Percent Advected: 34.1

Half-Lives (hr), (based upon Biowin (Ultimate) and Aopwin):
Air: 18.56
Water: 360
Soil: 720
Sediment: 3240

Biowin estimate: 3.048 (weeks)

Advection Times (hr):
Air: 100
Water: 1000
Sediment: 5e+004

Test substance : BBSA (CAS 3622-84-2)
Reliability : (2) valid with restrictions
23.05.2005 (5)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Type : aerobic
Inoculum : activated sludge
Concentration : 21.75 mg/l related to Test substance
21.8 mg/l related to Test substance
Contact time : 28 day(s)
Degradation : ca. 18 (±) % after 28 day(s)
Result :
Deg. product :
Method : OECD Guide-line 301 B "Ready Biodegradability: Modified Sturm Test (CO_2 evolution)"
Year : 2001
GLP : yes
Test substance :

Method : INOCULUM
- Inoculum: activated sludge from sewage treatment plant Waterschap de Maaskant, 's-Hertogenbosch, The Netherlands
- Preparation of inoculum: concentrated sludge (6.5 g solids/L) was left to settle for 30 min; the decanted liquid was used as inoculum (7.65 ml/L mineral medium)

TEST SYSTEM
- Preparation of test solution: mineral solution and inoculum were added to the bottle and aerated overnight with CO_2-free air; the test substance was added and the volume was made up to 2 L with Milli-RO water.
- Initial test substance concentration (mg CO_2/L): 45.0 mg/L and 45.2 mg/L
- Culturing apparatus: 2 L brown glass bottles
- Number of culture flasks per concentration: 2 with test substance and inoculum, 2 with inoculum, 1 with reference substance and inoculum, 1 with test substance, reference substance and inoculum
- Aeration: yes, ca. 30-100 ml/min
- Test duration: 28 days
- Sampling: on day 1, 4, 6, 8, 11, 14, 18, 22, 26 and 28
- Analytical parameter: CO_2 evolution
- ThCO_2: 2.07 mg CO_2/mg test substance

TEST CONDITIONS
- Composition of mineral solution: according to guideline
- Test temperature: 20-23 °C

REFERENCE SUBSTANCE: 40.2 mg sodium acetate/L

Result	:	10-day window reached: no Mean % biodegradation corrected for blank was 23 and 12% for 21.75 and 21.8 mg/L of test substance after 28 days Differences in replicate values at end of test: 11% REFERENCE SUBSTANCE: 105% after 28 days
Test substance	:	BBSA (CAS 3622-84-2), purity 99.8%.
Reliability	:	(1) valid without restriction The concentration of suspended solids in the concentrated sludge of 6.5 g/L instead of 3-5 g/L is not thought to have influenced the outcome of the test.

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3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type	:	static
Species	:	Daphnia magna (Crustacea)
Exposure period	:	48 hour(s)
Unit	:	mg/l
EC50	:	= 56
Analytical monitoring	:	no
Method	:	OECD Guide-line 202
Year	:	2001
GLP	:	yes
Test substance	:	

Method :

TEST ORGANISMS
- Species: Daphnia magna
- Source/supplier: in-house bred
- Breeding method: after 7 days of cultivation half of the medium was renewed twice a week; maximum age of culture: 4 weeks
- Age: < 24 h
- Feeding (pretreatment): fresh algae
- Feeding during test: none

STOCK AND TEST SOLUTION AND THEIR PREPARATION: 100 mg of test substance in 1 L of medium was treated with ultrasonic waves for 10 minutes to yield a clear and colourless solution

DILUTION WATER
- Source: milli-RO water
- Hardness: 250 mg CaCO3/L
- Ca/Mg ratio: 4
- pH: 8.0 ± 0.2

TEST SYSTEM
- Test type: static
- Concentrations: 0, 10, 18, 32, 56 and 100 mg/L (based on range-finding test)
- Exposure vessel type: 100 ml glass vessel
- Number of individuals: 10 per replicate, 2 replicate/treatment
- Photoperiod (intensity of irradiation): 16 h light; 8 h dark
- Test duration: 48 hours
- Test parameter: immobility
- Observation times: at 24 and 48 hours

PHYSICAL MEASUREMENTS
- Measuring times: pH and dissolved oxygen at the beginning and end of the test for all concentrations and control; temperature daily in one control vessel beginning at the start of the test
- Test temperature: 19.9-21.5 °C
- Dissolved oxygen: 8.4-8.7 mg/L (93-97%)
- pH: 7.9-8.1

REFERENCE SUBSTANCE: potassium dichromate

STATISTICAL METHODS: Probit (Finney)

Result : RESULTS

- Nominal concentrations: 0, 10, 18, 32, 56 and 100 mg/L
- Measured concentrations (mg/L): not performed
- Immobility: 0/20, 0/20, 0/20, 2/20, 6/20 and 20/20 at 48 h
- Dose related effects: yes
- Remark: at 32 and 56 mg/L 1/20 and 5/20 were trapped at the surface of the test solution

RESULTS REFERENCE SUBSTANCE
- Concentrations: 0, 0.10, 0.18, 0.32, 0.56, 1.0 and 1.8 mg/L
- Results: 0, 0, 0, 0, 0, 10/10 and 10/10

Test substance : BBSA (CAS 3622-84-2), purity 99.8%.
Reliability : (2) valid with restrictions
As requested the study was performed without analytical support.

23.05.2005 (10)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species	:	Selenastrum capricornutum (Algae)
Endpoint	:	growth rate
Exposure period	:	72 hour(s)
Unit	:	mg/l
NOEC	:	= 10
EC50	:	= 83
Limit test	:	no
Analytical monitoring	:	no
Method	:	OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year	:	2001
GLP	:	yes
Test substance	:	

Method :

TEST ORGANISMS
- Species: Selenastrum capricornutum
- Source/supplier: in-house culture
- Laboratory culture: yes
- Pretreatment: 4 days under test conditions at 2E4 cells/ml
- Initial cell concentration: 1E4 cells/ml

STOCK AND TEST SOLUTION AND THEIR PREPARATION: 100 mg of test substance in 1 L of medium was treated with ultrasonic waves for 10 minutes followed by stirring for 5 minutes to yield a clear and colourless solution

DILUTION WATER
- Source: milli-Q water

GROWTH/TEST MEDIUM CHEMISTRY
- M2-medium
- Hardness: 24 mg CaCO3/L

TEST SYSTEM
- Concentrations: 0, 2.2, 4.6, 10, 22, 46 and 100 mg/L
- Exposure vessel type: 100 ml glass vessel
- Number of replicates: 3 for test solution, 6 for blank control
- Photoperiod (intensity of irradiation): continuously (4000-9000 lux with max. 20% variation)
- Test duration: 72 hours
- Test parameter: cell density measured by spectrophotometry at 720 nm
- Observation times: at 0, 24, 48 and 72 hours

PHYSICAL MEASUREMENTS

- Measuring times: pH at beginning and end of the test; temperature every day in a temperature-control vessel
- Test temperature: 22.3-23.5 °C
- pH: 8.0-8.3

REFERENCE SUBSTANCE: potassium dichromate

STATISTICAL METHOD: ANOVA, Tukey test, Bonferroni t-test

Result : RESULTS
- Nominal concentrations: 0, 2.2, 4.6, 10, 22, 46 and 100 mg/L
- Cell density data: 96.8, 106.7, 87.0, 76.7, 69.2, 28.2 and 6.0 xE4 cells/ml at 72 hours
- Inhibition growth rate (% of control): -2, 2.3, 5.1, 7.4, 27.3 and 61.1
- Inhibition biomass (AUC) (% of control): -8.6, 5.1, 13.5, 23.8, 63.6 and 93.1

GROWTH FACTOR CONTROL: 97

RESULTS REFERENCE SUBSTANCE
- Concentrations: 0.18, 0.32, 0.56, 1.0, 1.8 and 3.2 mg/L
- Results growth rate: 1.9, 2.0, 9.1, 42.0, 83.7 and 98.6% of control

Test substance : BBSA (CAS 3622-84-2), purity 99.8%.
Conclusion : 72 hr-ECr50 = 83 mg/L (95% CI 69-97 mg/L)
Reliability : (2) valid with restrictions
As requested the study was performed without analytical support.

23.05.2005 (11)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

In Vitro/in vivo	:	In vivo
Type	:	Distribution
Species	:	rat
Number of animals		
Males	:	
Females	:	20
Doses		
Males	:	
Females	:	1 mg/kg
Vehicle	:	
Route of administration	:	i.v.
Exposure time	:	
Product type guidance	:	
Decision on results on acute tox. tests	:	
Adverse effects on prolonged exposure	:	
Half-lives	:	1st.: 2nd.: 3rd.:
Toxic behaviour	:	
Deg. product	:	
Method	:	
Year	:	1997
GLP	:	no data
Test substance	:	other TS

Method : 20 female Wistar rats received radiolabelled BBSA (13C, 1 mg/kg i.v.) and were sacrificed 1, 2 or 5 minutes or 4, 8 or 24 hours after administration (4 animals/time point).
Tissue samples were collected at all time points except at the 24-hour sacrifice
Blood samples were taken after 1, 5, 15, 30 and 60 minutes and after 4, 8 and 24 hours.
The amount of radiolabelled material in liver, kidneys, skeletal muscle and body fat was determined by GC-MS
(background levels of unlabelled BBSA were subtracted).

Method recovery (4 samples):
Plasma: 72% (at 10 ng/mL), 96% (at 100 ng/mL)
Blood: 72% (at 10 ng/mL), 83% (at 100 ng/mL)
Liver: 99% (at 50 ng/g)
Kidney: 104% (at 50 ng/g)
Muscle: 98% (at 50 ng/g)
Fat: 96% (at 50 ng/g)
Brain: 100% (at 50 ng/g)

Remark : The study design is described very shortly and its contents is limited to the above mentioned.

Result : Amount of 13C-BBSA:

Liver:
maximum 3130 ng/g (2 min); declining to 3.75 ng/g (8 h)

Kidney:
maximum 1338 ng/g (1 min); declining to 3.63 ng/g (8 h)

Skeletal muscle:
maximum 1044 ng/g (2-5 min); declining to 3.26 ng/g (8 h)

Peri-renal fat:
maximum 3130 ng/g (5 min); declining to 2.92 ng/g (8 h)

Plasma:
maximum 603 ng/mL (1 min); declining to 9.55 ng/mL (24 h)

The ratio tissue:plasma 13C-BBSA (taking into account the perfusion rate) increased more than 3 fold during the first 5 minutes (from 2.86 to 10.4) for all tissues investigated and declined within 4 hours to <<1.0 for all tissues except fat. For adipose tissue this level (<<1.0) was reached after 8 hours.

The following pharmacokinetic parameters were calculated from the plasma curve for 13C-BBSA:

T1/2 distribution phase:	0.78 min
T1/2 intermediate phase:	11 min
T1/2 terminal phase:	1036 min
Mean residence time:	1306 min
Plasma clearance:	5.03 mL/min
Blood clearance:	2.65 mL/min
Distribution volume (steady state):	6571 mL
Elimination rate constant (steady state:	7.7E-04

Test substance : BBSA (CAS 3622-84-2), 13C-labelled.
No details known.

Conclusion : The highest levels of 13C BBSA in peripheral tissue are attained during the first 2 minutes after administration.
For both high perfusion organs (liver and kidney) and low perfusion organs (muscle and fat) the tissue profiles are similar.
Plasma levels decline rapidly and distribution volume is high.

22.01.2002 (12)

In Vitro/in vivo : In vivo
Type : Distribution
Species : rat
Number of animals
Males : 15
Females :
Doses
Males : 1 mg/kg bw
Females :
Vehicle :
Route of administration : i.v.
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product :
Method :
Year : 1997
GLP : no data
Test substance : other TS

Method : 15 male Sprague Dawley rats received BBSA (1 mg/kg i.v.) and were sacrificed 1, 5, 15, 30 or 60 minutes after administration (3 animals/time point). Tissue and blood samples were taken after 1, 5, 15, 30 and 60 minutes.
The amount of BBSA in right partial cortex, cerebellum, spinal cord, cerebrospinal fluid, skeletal muscle, peri-renal fat, kidney and liver was

determined by GC-MS
(background levels of unlabelled BBSA were subtracted).

Method recovery (4 samples):
Plasma: 72% (at 10 ng/mL), 96% (at 100 ng/mL)
Blood: 72% (at 10 ng/mL), 83% (at 100 ng/mL)
Liver: 99% (at 50 ng/g)
Kidney: 104% (at 50 ng/g)
Muscle: 98% (at 50 ng/g)
Fat: 96% (at 50 ng/g)
Brain: 100% (at 50 ng/g)

Result : In blood, liver, kidney, skeletal muscle and peri-renal fat values found were in good agreement with that from the experiment with radiolabelled material.
In cortex (maximum 1781 ng/g), cerebellum (maximum 1830 ng/g)) and spinal cord (maximum 1605 ng/g) BBSA content was highest in the first minute following administration. The same was true for the cerebrospinal fluid (maximum 203 ng/mL). BBSA content declined gradually (and in parallel) for all CNS tissues.

The ratio cerebrospinal fluid:blood BBSA was ~0.28 during the duration of the experiment.

Test substance : BBSA (CAS 3622-84-2), purity not indicated.

Conclusion : In view of the parallel decline and the constant CSF:blood ratio, it is concluded that BBSA passes the blood - CSF barrier passively.

22.01.2002 (12)

In Vitro/in vivo : In vivo
Type : Excretion
Species : rat
Number of animals
Males :
Females : 4
Doses
Males :
Females : 1 mg/kg bw
Vehicle : other: condensed milk
Route of administration : oral unspecified
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st:
2nd:
3rd:
Toxic behaviour :
Deg. product :
Method :
Year : 1997
GLP : no data
Test substance : other TS

Method : Oral administration of unlabelled BBSA (1 mg/kg bw) was followed by 13C-BBSA (1 mg/kg bw in 0.9% saline) via lateral tail vein (intermediate time not indicated).
Urine was collected over 24 hours.

Result : Urinary excretion after oral administration was 1.09-1.69 ng/mL (control values from untreated animals were 1.32-3.13 ng/mL).
The fraction of 13-BBSA excreted was 0.007-0.034%.

BBSA-OH was identified in urine by CID analysis.

Test substance : BBSA (CAS 3622-84-2), purity not indicated.

13C-BBSA (CAS 3622-84-2), purity not indicated.

Conclusion : Due to the very low recovery calculation of oral bioavailability was not possible.

22.01.2002 (12)

In Vitro/in vivo : In vivo
Type : Toxicokinetics
Species : rat
Number of animals
Males :
Females : 4
Doses
Males :
Females : 1 mg/kg bw
Vehicle : other: condensed milk
Route of administration : oral unspecified
Exposure time :
Product type guidance :
Decision on results on acute tox. tests :
Adverse effects on prolonged exposure :
Half-lives : 1st.:
2nd.:
3rd.:
Toxic behaviour :
Deg. product :
Method :
Year : 1997
GLP : no data
Test substance : other TS

Method : test 1
Oral administration of unlabelled BBSA was followed by 13C-BBSA (1 mg/kg bw in 0.9% saline) via the lateral tail vein. Blood was collected from a silastic/polyethylene catheter over 24 hours.

test 2
13C-BBSA (1 mg/kg bw in 0.9% saline) was administered via the lateral tail vein. Blood was collected from a silastic/polyethylene catheter over 24 hours.

Result : test 1
Oral bioavailability was 52-79% (mean 62%), calculated as the ratio under the plasma concentration time curves following simulatanous administration of native and radiolabelled.
Plasma concentration curves were 3-phasic with mean half-lives of: 0.32, 27 and 500 minutes, respectively. Mean residence time was 183 min.
Blood and plasma clearance were 13 and 7 mL/min, respectively.

test 2
Plasma concentration curves were 3-phasic with mean half-lives of: 0.34, 29 and 480 minutes, respectively. Mean residence time was 313 min.
Blood and plasma clearance were 11 and 5.5 mL/min, respectively.

Both tests (mean values):
Distribution volume: 7.6 L
Steady state distribution volume: 2.7 L
Steady state elimination constant: 0.009

Test substance : BBSA (CAS 3622-84-2), purity not indicated,
13C-BBSA, no details provided.

22.01.2002 (12)

In Vitro/in vivo :
Type : Absorption

Species	:	rat
Number of animals		
Males	:	3
Females	:	
Doses		
Males	:	
Females	:	
Vehicle	:	
Method	:	other: in-situ brain perfusion
Year	:	1997
GLP	:	no data
Test substance	:	other TS

Method : A polyethylene catheter was implanted in the right external carotid artery of 3 rats. 13C-BBSA in iso-osmotic saline or serum (0.5 ug/mL) was infused for 13 or 15 seconds and complete perfusion of the right cerebral hemisphere was ensured. The perfusion was terminated by decapitation of the animal and a sample of the perfusate was collected and analysed. Samples of the right frontal, partietal and occipital corties were removed and analysed for 13-BBSA.

Determinations:
total brain content, extravascular content, uptake rate (Kin).

Result : test 1 (15 min perfusion in saline)

Mean extravascular 13C-BBSA (ng/g):
856 (right frontal cortex), 1059 (right parietal cortex) and 1029 (right occipital cortex)

Mean Kin (mL/s/g):
0.108(right frontal cortex), 0.137 (right parietal cortex) and 0.134 (right occipital cortex)

Mean extraction (%):
98 (right frontal cortex), 125 (right parietal cortex) and 122 (right occipital cortex)

test 2 (30 min perfusion in saline)

Mean extravascular 13C-BBSA (ng/g):
1500 (right frontal cortex), 1496 (right parietal cortex) and 1304 (right occipital cortex)

Mean Kin (mL/s/g):
0.088 (right frontal cortex), 0.087 (right parietal cortex) and 0.076 (right occipital cortex)

Mean extraction (%):
80 (right frontal cortex), 79 (right parietal cortex) and 69 (right occipital cortex)

test 3 (15 min perfusion in serum)

Mean extravascular 13C-BBSA (ng/g):
455 (right frontal cortex), 412 (right parietal cortex) and 259 (right occipital cortex)

Mean Kin (mL/s/g):
0.071 (right frontal cortex), 0.062 (right parietal cortex) and 0.038 (right occipital cortex)

Mean extraction (%):

63 (right frontal cortex), 57 (right parietal cortex) and 37 (right occipital cortex)

Test substance : BBSA (CAS 3622-84-2), 13C-labelled.
No details known.

Conclusion : After 15 seconds saline perfusion time Kin approximates perfusion rate to the brain (0.11 mL/s/g) and BBSA is almost completely extracted.
The Kin values decreased after 30 seconds of saline perfusion. This may have been caused by backflow or by binding of 13C-BBSA to the vascular epithelia.
In the plasma perfusion experiment Kin is decreased 35-70% compared to values for saline perfusion (15 min). This may be explained by binding of 13C-BBSA to plasma proteins.

Concluding BBSA seems to penetrate the brain easily and the cerebrovasculature does not present a barrier.

22.01.2002 (12)

In Vitro/in vivo : In vitro
Type : Metabolism
Species : rat
Number of animals
Males :
Females :
Doses
Males :
Females :
Vehicle :
Method :
Year : 1997
GLP : no data
Test substance : other TS

Method : Liver homogenates were prepared from Aroclor-1254 induced and non induced male Fisher rats, non-induced New Zealand White female rabbits and samples of (donor) human liver. BBSA (1 mM or 200 ug) was incubated in liver homogenates during 4 hours. Incubates contained cytochrome P-450, NADPH, glucose-6-phosphate, MgCl2, glucose-6-phosphate dehydrogenase and potassium phosphate buffer. Controls were run in absence of NADPH.
Selected incubates also contained glutathione or uridine diphosphate glucuronic acid.

Samples were analysed for the presence of metabolites by GC-MS after reconstitution with a derivatising mixture of bis(trimethylsilyl)trifluoroacetamide:acetonitrile (30:20).

Result : In rat (induced or non-induced), rabbit and human liver homogenate BBSA was metabolised to 2-hydroxy-n-butylbenzenesulphonamide (BBSA-OH hydroxyl group on the second atom of the butyl side chain). No other Phase I metabolites were identified. In presence of Phase II enzymes no conjugation was observed.

Test substance : BBSA (CAS 3622-84-2), purity not indicated

Conclusion : BBSA metabolism in vitro cytochrome P-450 dependent. No indications for Phase II metabolism were present.
In vivo, however, it may be possible that BBSA and BBSA-OH are subject to glucuronidation or acetylation.

22.01.2002 (12)

5.1.1 ACUTE ORAL TOXICITY

Type : LD50

Value	:	= 2070 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	20
Vehicle	:	
Doses	:	1.26, 2.0, 3.2 g/kg bw
Method	:	Directive 92/69/EEC, B.1
Year	:	1996
GLP	:	yes
Test substance	:	

Method :

TEST ANIMALS:
- Species/strain: Sprague-Dawley rat
- Source: Harlan Olac Ltd, Bicester, Oxon, England
- Age: 4-7 weeks
- Number: 5/sex at 2.0 g/kg bw followed by 5 males at 1.26 and 3.2 mg/kg bw
- Weight at study initiation: 87-108 g for males and 93-99 g for females
- Controls: no

ADMINISTRATION
- Doses: 1.26, 2.0 and 3.2 g/kg bw
- Route: gavage
- Volume administered: <=2.8 ml/kg bw

EXAMINATIONS: see results (observation period 14 days)

STATISTICAL METHOD: Probit analysis (Finney)

Result :

MORTALITY
- Number of deaths at each dose: 2/5 males and 1/5 females at 2.0 g/kg bw and all rats at 3.2 g/kg bw
- Time of death: between 26 and 45 hours of dosing

CLINICAL SIGNS: piloerection and hunched posture in all animals at all doses; lethargy, partially closed eyelids, abnormal gait and prostration at all doses; decreased respiratory rate, pallor of the extremities, increased lacrimation and tremors at 1.26 and 3.2 g/kg bw; cold body surfaces at 2.0 and 3.2 g/kg bw; increased urine production at 2.0 g/kg bw; clonic convulsions, comatose state and dark green stained urine at 3.2 g/kg bw

BODY WEIGHT GAIN: body weight loss in all animals that died; decreased body weight gain on day 8 at 2.0 g/kg bw

NECROPSY FINDINGS:
- 3.2 g/kg bw: congestion in the heart, lungs, liver, kidneys, stomach, intestines, shrunken appearance of stomach, splenic atrophy, congestion and pale subcutaneous tissue, congestion, red fluid contents and prominent blood vessels in the brain, and green/black fluid contents in the urinary bladder (1 animal)
- 2.0 g/kg bw: congestion and yellow staining in the stomach (1 female decendent)
- 1.26 g/kg bw: shrunken appearance and inflammation of stomach in all males

Test substance	:	BBSA (CAS 3622-84-2), purity 99.9%.
Conclusion	:	LD50 = 2.07 g/kg bw (95% CI 1.74-2.46)
Reliability	:	(1) valid without restriction

30.05.2005 (13)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	> 4066 mg/m³
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	40
Vehicle	:	
Doses	:	0, 3431, 3439 and 4066 mg/m3
Exposure time	:	4 hour(s)
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	1991
GLP	:	yes
Test substance	:	

Method :

TEST ANIMALS
- Species/strain: Wistar rat
- Source: Winkelmann, Borchen, Kreis Paderborn
- Age: 2-3 months
- Weight at study initiation: ca. 180-210 g
- Number of animals: 5/sex/concentration
- Controls: yes (3-monthly)

ADMINISTRATION
- Type of exposure: nose-only
- Exposure duration: 4 hours
- Concentrations (nominal): 0, 57500 and 115000 mg/m3
- Concentrations (measured): 0, 3431 and 4066 mg/m3
- Particle size: 89-99% <=3 µm; MMAD = 1.37-1.75 and GSD = 1.44-1.55 (Aerodynamic Particle Sizer with Laser-velocimeter)
- Type of particles: aerosol (spraying of undiluted substance)
- Air changes: ca. 30/hour

EXAMINATIONS: see results (observation period 14 days)

ANALYSES
- Method: gaschromatography with flame ionisation detection
- Sampling times: 3 times during exposure

STATISTICAL METHOD: not applicable

Remark : Due to an error in analysis of the test substance nominal concentration at 115000 mg/m3 a second group was tested at this concentration (only results of this second group are reported).

Result : ANALYSIS: The large difference between nominal and measured concentration was reported to be due to pre-separation of the larger particles.

MORTALITY
- Number of deaths: none

CLINICAL SIGNS:
- 3439 mg/m3: abnormal gait, piloerection, laboured respiration, bloody snout
- 4066 mg/m3: piloerection

All animals recovered within 1 day.

BODY WEIGHT GAIN: no treatment-related effect

NECROPSY FINDINGS: no treatment-related effect

Test substance : BBSA (CAS 3622-84-2), purity 99.8%.

Reliability : (1) valid without restriction
30.05.2005 (14)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 2000 mg/kg bw
Species	:	rat
Strain	:	Sprague-Dawley
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: none
Doses	:	2000 mg/kg bw
Method	:	Directive 92/69/EEC, B.3
Year	:	1995
GLP	:	yes
Test substance	:	

Method :
TEST ANIMALS
- Source: Harlan Olac Ltd, Bicester, England
- Age: 7-10 weeks
- Weight at study initiation: 220-250 g
- Number of animals: 5/sex/dose

ADMINISTRATION
- Area covered: ca. 25 cm2
- Occlusion: yes
- Vehicle: none
- Total volume applied: 1.8 ml/kg bw
- Doses: 2000 mg/kg bw
- Removal of test substance: after 24 hours with warm water

EXAMINATIONS: see results (observation period 15 days)

Result : MORTALITY: none

CLINICAL SIGNS: none

BODY WEIGHT GAIN: lower body weigth gain for one male and one female on day 8

NECROPSY FINDINGS: none

Test substance : BBSA (CAS 3622-84-2), purity 99.9%.
Reliability : (1) valid without restriction
23.05.2005 (15)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

5.2.2 EYE IRRITATION

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type	:	Sub-acute
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	28 days
Frequency of treatm.	:	daily
Post exposure period	:	no
Doses	:	50, 150 and 1000 mg/kg bw
Control group	:	yes, concurrent vehicle
NOAEL	:	= 50 mg/kg bw
Method	:	OECD Guide-line 407 "Repeated Dose Oral Toxicity - Rodent: 28-day or 14-d Study"
Year	:	2003
GLP	:	yes
Test substance	:	

Method :

TEST ANIMALS
- Strain: Wistar
- Source: Charles River Deutschland, Sulzfeld, Germany
- Age: ca. 6 weeks
- Weight at study initiation: 190-215 g for males and 154-180 g for females
- Number of animals: 5/sex/dose

ADMINISTRATION / EXPOSURE
- Exposure period: 28 days
- Route of administration: oral gavage
- Vehicle: propylene glycol
- Volume administered: ca. 5 ml/kg bw
- Post exposure period: none
- Doses: 0, 50, 150 and 1000 mg/kg bw

CLINICAL OBSERVATIONS AND FREQUENCY
- Mortality: twice daily
- Clinical signs: once daily
- Body weight: on days 1, 8, 15, 22 and 29 (females) or 30 (males)
- Food consumption: weekly
- Functional observations: during week 4 of treatment
- Haematology: at end of treatment
- Biochemistry: at end of treatment
- Ophthalmoscopy: at end of treatment

ORGANS EXAMINED AT NECROPSY (MACROSCOPIC AND MICROSCOPIC)
- Organ weights: adrenal glands, brain, epididymides, heart, kidneys, liver, spleen, testes, thymus
- Macroscopic: according to OECD 407
- Microscopic: according to OECD 407 + seminal vesicles from the control group and 150 and 1000 mg/kg bw group; liver, kidneys, testes, thymus and sciatic nerve were examined also at 50 mg/kg bw
- Other: brain perfusion and cranial part weighed

ANALYSES
- Method: HPLC with UV-detection at 220 nm
- Sampling times: last day of treatment

STATISTICAL METHODS: Dunnett-test, Steel-test, Fisher-test

Result : ANALYSES
- Accuracy: 98-105% of nominal concentration

- Stability: stable for 4 hours at roomtemperature
- Homogeneity: no difference in samples taken at different heights of formulation (98-105%)

TOXIC RESPONSE/EFFECTS BY DOSE LEVEL
- Mortality and time to death: one female at 1000 mg/kg bw died spontaneously on day 15 and the other males and females were killed in extremis between day 8 and 18
- Clinical signs: lethargy, hunched posture, uncoordinated movements, abnormal gait, salivation, emaciation and laboured respiration at 1000 mg/kg bw
- Body weight gain: all animals at 1000 mg/kg lost weight or showed reduced weight gain
- Food consumption: reduced at 1000 mg/kg bw
- Functional observation: no treatment-related changes
- Ophthalmoscopic examination: not reported
- Haematology: erythrocyte count was significantly decreased in males at 150 mg/kg bw (6%) and haemoglobin was decreased in males at 50 and 150 mg/kg bw (7%; 150 mg/kg bw significant)
- Clinical chemistry: no treatment-related effects
- Organ weights: absolute and relative kidney weight was increased at 150 mg/kg bw (21-24%) in males; absolute (19-29%) and relative (53-65%) testes weight was increased at 50 and 150 mg/kg bw
- Gross pathology:
1000 mg/kg bw: reduced size of prostate, seminal vesicles and epididymides; reduced size of spleen in 3 males and 1 female; reduced size of thymus in all males and 3 females; enlarged adrenal glands in all animals; enlarged liver in one male and one female and red or gray-white foci and/or dark red discolouration of the liver in one other male and female
150 mg/kg bw: enlarged liver in one male; enlarged kidney and pelvic dilatation in two males
- Histopathology:
1000 mg/kg bw: centrilobular hypertrophy of hepatocytes in all animals; multifocal necrosis in the liver in one male and one female; slight to marked hyaline droplet formation in duct epithelium of renal papilla in most animals and deposits of hyaline droplets in cortical tubular epithelium in some males; cortical fatty changes in adrenal glands of all males and cortical hypertrophy in all females; atrophy of the white pulp of the spleen in 2 males and 2 females; cortical atrophy of the thymus in almost all animals; minimal degenerating fibres of the sciatic nerve and in the ventral funiculi of the cervical cord in some animals; reduced secretion of prostate and seminal vesicles in all males.
150 mg/kg bw: slight centrilobular hypertrophy of hepatocytes in 2 males and 3 females and slight multifocal necrosis in one male; hyaline droplets in cortical tubular epithelium of the kidney in all males; cortical atrophy and cortical lymphocytolysis of thymus in one male; minimal degenerating fibres of the sciatic nerve in 2 males.
50 mg/kg bw: hyaline droplets in cortical tubular epithelium of the kidney in 3 males.

Test substance : BBSA (CAS 3622-84-2), purity 99.6%.

Conclusion : The slight haematological deviations which occurred only in males were not considered to be treatment related. Hyaline droplets in the kidney is considered to be specific for male rats and not relevant to humans.
The NOAEL = 50 mg/kg bw based on effects on liver and low incidence of degenerating nerve fibres.

Reliability : (1) valid without restriction
23.05.2005

(16)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA98, TA100, TA 1535, TA1537 and TA1538
Test concentration	:	50, 150, 500, 1500 and 5000 µg/plate
Cytotoxic concentr.	:	5000 µg/plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	other: mainly according to OECD471
Year	:	1983
GLP	:	no
Test substance	:	

Method :

TEST SYSTEM
- Species/cell type: Salmonella typhimurium TA98, TA100, TA 1535, TA1537 and TA1538
- Deficiency: histidine
- Metabolic activation system: Aroclor 1254 induced rat liver S9-mix

ADMINISTRATION
- Dosing: 50, 150, 500, 1500 and 5000 µg/plate
- Number of replicates: 3
- Application: plate incorporation
- Positive control groups and treatment:
  1) 2-aminoanthracene (+S9-mix; TA98, TA100, TA 1535, TA1537 and TA1538)
  2) 9-aminoacridine (TA1537)
  3) sodium azide (TA100 and TA1535)
  4) 2-nitrofluorene (TA98 and TA1538)
- Negative control group: DMSO

DEVIATIONS FROM GUIDELINE: Only Salmonella typh. strains were tested and no E. coli.

CRITERIA FOR EVALUATING RESULTS: positive if a statistically significant dose-related increase in the number of revertant colonies is obtained in two separate experiments

Result : GENOTOXIC EFFECTS
- With metabolic activation: negative
- Without metabolic activation: negative

PRECIPITATION CONCENTRATION: >5000 µg/plate

CYTOTOXIC CONCENTRATION
- With metabolic activation: 5000 µg/plate
- Without metabolic activation: 5000 µg/plate

Test substance	:	BBSA (CAS 3622-84-2), purity 99.5%.
Reliability	:	(2) valid with restrictions Non-GLP study.

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5.6 GENETIC TOXICITY 'IN VIVO'

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

Endpoint	:	Cytotoxicity
Study descr. in chapter	:	
Reference	:	
Type	:	other: in vitro
Species	:	
Sex	:	
Strain	:	
Route of admin.	:	
No. of animals	:	
Vehicle	:	
Exposure period	:	
Frequency of treatm.	:	
Doses	:	
Control group	:	
Observation period	:	
Result	:	toxic
Method	:	
Year	:	1993
GLP	:	no data
Test substance	:	other TS

Method :

Neuro-2a and C6 glioma cells were plated at a density of 2E05 and 2.5E03 cells per well on 6 or 12 wells plates.

test 1
After 24 hours 10-500 uM BBSA was added and cells were incubated for 72 hours. Viability was assessed using the tryptan blue dye-exclusion method. All determinations were done in triplicate.

test 2
Cells were incubated for 72 hours in presence of 10-500 uM BBSA. Cell death was assessed by measuring LDH levels. All determinations were done in triplicate.

test 3
Cells were incubated for 72 hours in presence of 10-500 uM BBSA. 3[H]thymidine was added during 4 hours and incorporation was measured to assess effects on DNA synthesis. All determinations were done in quadruplicate.

test 4
Cells were incubated for 72 hours in presence of 10, 100 and 250 uM BBSA. Immunoreactivity was measured with antibodies against glial fibrillary acidic protein and S100 protein (C6-glioma cells) and 160 kDa neurofilament subunit protein (neuro-2a cells).

Result :

test 1
Neuro-2a cells
10 uM BBSA gave 50% cell death at 72h
50 uM BBSA gave 30% cell death at 24h and 90% at 72h
500 uM BBSA gave 100% cell death at 72h

C6-glioma cells
100 uM BBSA gave 50% cell death at 72h
500 uM BBSA gave 90% cell death at 72h

test 2
positive correlation between concentration and LDH release for both neuro-2a cells and C6-glioma cells

test 3
Neuro-2a cells
20 uM BBSA inhibits DNA synthesis by 70% at 72h
C6-glioma cells
10 uM BBSA inhibits DNA synthesis by 18% (24h) and 30% (72h)
250 uM BBSA inhibits DNA synthesis by 70% at 72h

test 4
reduced immunoreactivity with increasing concentrations in both cell lines

Test substance : BBSA (CAS 3622-84-2), purity not indicated
Conclusion : BBSA is toxic to cells of neuronal and glial origin in vitro. Cells of neuronal origin are 10 times more sensitive. The toxicity of BBSA is cell specific.

22.01.2002 (18)

Endpoint : Neurotoxicity
Study descr. in chapter :
Reference :
Type :
Species : rat
Sex : male
Strain : Wistar
Route of admin. : i.p.
No. of animals : 30
Vehicle : other: olive oil
Exposure period :
Frequency of treatm. : every 6 hours
Doses : 300 mg/kg bw
Control group : other: see freetext method
Observation period :
Result :
Method :
Year :
GLP : no data
Test substance : other TS

Method : TEST ORGANISMS
- Mean weight: 302 g
- Number of animals: 6/treatment

ADMINISTRATION / EXPOSURE
- Exposure period: 24-42 hours
- Route of administration: i.p.
- Dose: 300 mg/kg bw every 6 hours
- Vehicle: olive oil
- Dosing volume: 5 mL/kg

test 1 (total 7 treatments)
Untreated and vehicle treated controls.
Clinical signs 20 min after each treatment including: gait, righting reflex, straightening of the tail during walking and coma.
Necropsy including histopathology on stomach, liver, kidney and urinary bladder.

test 2 (total 4 treatments)

Untreated controls.
Monitoring in an Animal Activity Meter 20 minutes and 2 hours after each treatment.

test 3 (total 4 treatments)
Untreated controls, 3 rats/treatment.
Immuhistochemical determination of anti-acetylcholinetransferase antibodies in the lumbar spinal cord (light microscopic quantitative image analysis) in 2 rats 2 hours after the last treatment.

Result : test 1
No information on mortality.
Staggering gait, hindlimb paresis, hindlimb splaying, bed chewing, eating with pecking movements and self paw-biting appeared, increasing in severity with time. Response to sudden stimuli was decreased.
At necropsy urinary bladder was filled with bloody urine and forestomach was hemorrhagic and ulcerative. Microscopically this was accompagnied by leukocyte infiltrations in the epithelium and dilauted blood vessels in the subserosal layers. In the kidney slight infiltration of erythrocytes in the interstitial spaces of the medullary portion (no necrosis).

test 2
Changes in motor activity consisted of decreased repetition of the same movement type (warm-up of new surrounding) after the first exposure compared to control animals. Total ambulatory count was decreased 20 minutes after all exposures and 2 hours after the first exposure. In control animals increased activity after the first "exposure" was followed by shut down. This effect was less clear in treated animals.

test 3
Alpha-motor neurons in lamina IX of the lumbar spinal cord of treated animals showed decreased immunohistochemical staining.

Test substance : BBSA (CAS 3622-84-2), purity not indicated; 6% (v/v) solution in olive oil

Conclusion : Toxic signs after i.p. exposure to BBSA were CNS depression, hindlimb paresis with splaying, pica, teeth-grinding and self paw-biting. Decreased motor activity can be related to decreased activity of acetylcholine transferase in the lower motor neurons.

22.01.2002 (19)

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

(1) DIN SDS, Bayer, 2003.

(2) UCB Sicherheitsdatenblatt No 26/3.

(3) MSDS, Proviron, 2001.

(4) Proviron Fine Chemicals N.V. Oostende

(5) EPISUITE v.3.12, 2005

(6) MSDS, Proviron, 2000.

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT